CLINICAL MEDICINE

SEPTEMBER, 1952

VOLUME 59, NO. 9

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1. *Seley, S. A.: Am. J. Dig. Dis. 13:238 (July) 1946.* 2. *Rossien, A. X.: Rev. of Gastroenterol. 16:34-52 (Jan.) 1949.* 3. *Rossien, A. X. and Victor, A. W.: Am. J. Dig. Dis. 14:226-229 (July) 1947.* 4. *Batterman, R. C. and Ehrenfeld, I.: Gastroenterol. 9:141 (August) 1947.*

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TABLE of CONTENTS

59th year of publication

Vol. 59, No. 9 September, 1952

EDITORIAL

ORIGINAL ARTICLES

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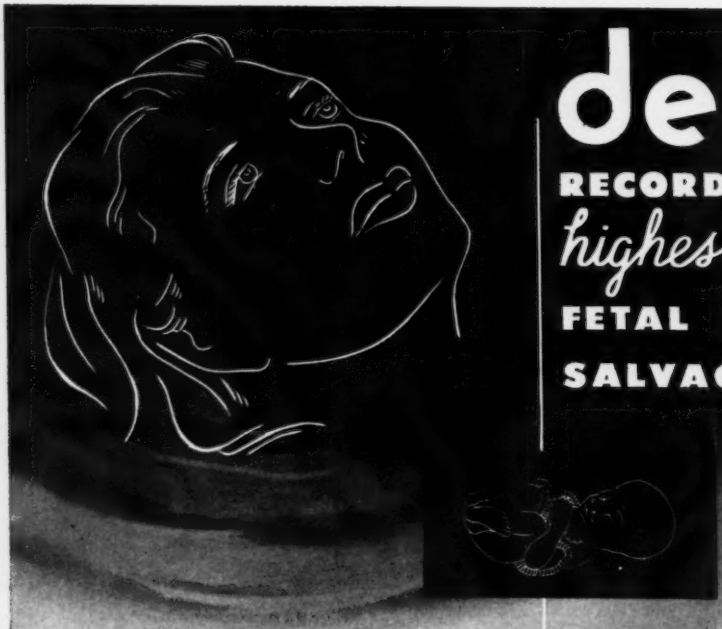

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Man in Numbers

FREDERIC R. STEARNS, M.D., *Editor*

How ever we form our concept of life in natural science, whether according to the chemical theory, the thermo-dynamic theory, or the electro-dynamic theory, in the totality of its manifestations it will always resist a comprehension in terms of quantities. Yet, the development of science in recent decades has exhibited that we can understand scientifically only in quantities, or expressed more specifically, only according to the laws of statistics and the calculus of probability. There we have the discrepancy between the qualitative aspect of life processes and the quantitative limitations of the range of science.

Thus, it has always been an intriguing vantage point from which to look at life quantitatively. We shall give a few examples, at random.

The human heart beats, on the average, 70 times a minute, 100,800 times a day and 2,575,440,000 times in a life span of 70 years. The blood vessels have a combined length of about 100,000 miles; the capillaries have, together, a surface area of one acre. The heart pumps with each beat five ounces of blood into the circulation, which amounts to 22 pints a minute, 1,500 pints an hour, and 4,000 gallons a day. The heart generates sufficient energy, within 2 hours, to lift a weight of 65 tons one foot in the air.

Each kidney has about 1,200,000 nephrons, each about 2 inches long, so that the combined length of all nephrons in an adult would amount to 75 miles. The length of individual capillaries in a glomerulus is about one inch; thus, the total of all capillaries in both kidneys would measure more than 37 miles. The entire filtering surface of all glomeruli exceeds twice the body surface.

In an adult there are approximately 300,000,000 alveoles in both lungs with an aggregate surface of 700 square feet. The adult absorbs more than 20 cubic feet of oxygen in 24 hours, and the blood releases more than 20 cubic feet of carbon dioxide within the same period.

There are 9 billion ganglion cells in the cerebral cortex and about 12 billion cells in the brain, altogether. The possible number of connections of two neurons in the human brain has been estimated as being 102,-783,000. While an electric current in a wire travels 11,160,000 miles a minute, the nerve impulses are conveyedo over the axons with a speed of not more than 4½ miles per minute.

It has been estimated that about 10,000,000 red blood cells are des-

troyed (and replaced) per second in an adult. The diameter of an erythrocyte is 0.007 mm. An adult is about 250,000 times taller in size than the diameter of an erythrocyte is long. A normal specimen of semen will contain a volume of 2 to 5 cc. and a count of 75 to 100 million spermatozoa per cc.

The adult has a total of 120,000 hairs on the average scalp; blond individuals have an average of 150,000 hairs and red haired individuals have only 90,000.

In a new born male infant there are 270 separate bony units, in a 14 year old boy 350 and in an adult man, 40 years of age, 206.

Seventy per cent of the weight of the human body is water; 50 per cent is intracellular water and 20 per cent, extracellular water. 170 liters of water are filtered from the blood plasma through the kidneys in a 24 hour period.

The average American adult consumes once every 50 days his own weight in food; a healthy child does so in about 10 days, while an old man does it only once in 65 days. In addition an adult breathes approximately one fifth of his own mass in air within 24 hours.

At the end of the first embryonic month the human body is about 8,000 times as heavy as at the beginning of this month. At the end of the second month the weight increase is 500 times the weight of the start of the second month; at the end of the third it is 11 times, and at the end of the fourth month four times, as much as at the beginning of the respective months. Yet, during a life span of 70 years the body multiplies its weight at birth by only 20 times.

It has been figured out that, according to future net-earnings, the money value of the average American individual would be: at age 20, $32,200 to $53,000; at age 40, $21,300 to $54,500; at age 50, $11,000 to $30,000, and at age 55, $6,100 to $18,700.

Another approach in calculating the individual money value of man was made in terms of energy. If the atoms which compose the human body could be transformed fully in energy a body, weighing 150 pounds, would have a money value of $85,500,000,000 as each pound would produce 11,400,000,000 kilowatt hours of energy, worth $570,000,000. These figures refer to the money value at the time before the dollar lost almost half of its purchasing power. The present figures are correspondingly higher. In order to counterbalance this overoptimistic view on the money value of the individual human body substance, the sober analytical chemical approach of another investigator resulted in the conclusion that the chemical substances which quantitatively make up the human body of a person have a market value of approximately 87 cents.

(Reprinted by request)

ORIGINAL ARTICLES

Anorectal Fistula: Office and Surgical Management

Acute anal cryptitis, cause of much anorectal disease, may be treated either in the physician's office or hospital

H. MARK YOUNG, M.D., *Los Angeles, California*

The recognition and treatment of fistulous processes in the anorectal area are predicated upon historic observations. In 1880, Herrmann described what he called "intramuscular sinuses and glands" extending into the sphincteric mechanism from the anal crypts of Morgagni.[1] As with much of the anatomic knowledge compiled in that period, its proper surgical application was not utilized for a full half century. In 1914, Franklin Paradise Johnson constructed accurate Borne wax models of the anal-rectal area, detailing the anal canal and the anal ducts and glands (intramuscular sinuses of Herrmann[2]). Emphasis is now placed upon these filaments which dip into the adjacent muscles of the anal sphincter from the anal crypts. It is felt that they are the precursors of fistulous pathways. These vestiges are better developed in certain persons who are more vulnerable to an infectious process developing in an anal crypt.

Embryonically, the prostatic glands, the para-urethral glands in the female, and the anal crypts and vestiges all develop from the cloacal membrane or plate.

ETIOLOGY

Clinical application of the foregoing is clarified when it is consider that acute anal cryptitis is the underlying factor in most cases of anorectal disease. Infection in an anal crypt is often preceded by an episode of diarrhea or trauma to this delicate and sensitive area. The valve becomes boggy and swollen, spasm of the anal sphincter ensues, and a focal infectious process develops within the confines of the crypt. If the causative organisms are virulent enough and the trap remains closed, the resulting exudate, pus and gas will push beyond these limits. If a pre-existing anal duct is present in the depths of the involved crypt, a path then exists for extention of the infection.[3] (Under the dissecting microscope, these ducts have been

1. Herrmann, G., and Defosses, L.: Sur la muquesuse de la region cloacale du rectum, *Compt. rend. Acad. d. sc.* 90: 1301, 1880.
2. Johnson, F. P.: The development of the rectum in the human embryo, *Am. J. Anat.* 16: 1, 1914.

followed into the external sphincter; more rarely, the ducts may extend superiorly into the submucosa of the rectum.[4])

SYMPTOMS

The patient's temperature usually is elevated. Throbbing pain is present and usually a tender mass may be noted adjacent to the anal orifice. This mass is the peri-anal abscess which originated in the anal crypt and pushed its way along a pre-existing path towards the integument. The process often takes several days. Infrequently, a hidden submucus perirectal abscess forms. Its presence is determined by careful digital rectal examination and is identified by one sector of the rectal ampulla bulging into the lumen.

TREATMENT

Office treatment — Treatment for peri-anal or rectal abscess constitutes a surgical emergency in that incision and adequate drainage must be instituted at once.

The patient usually is first examined in the physician's office. He is placed in a comfortable Sim's position and, with good light and gentle touch, the abscess is located. If it is definitely fluctuant and well circumscribed, the area is infiltrated with a 2 per cent solution of novocaine, and immediate drainage is effected through an ample tangential incision. The cavity is then loosely filled with iodoform gauze, to be removed the following day after a comforting Sitz bath.

SURGICAL TREATMENT

Surgical treatment is recommended if definite fluctuation is not apparent and a wide area of peri-anal induration and cellulitis is found. If the patient's medical history denotes that he has had the abscess for some time and if both peri-anal and rectal fluctuation are present, hospitalization and operation are recommended. In these cases, it will be found that the abscess has extended from the crypt to the tough peri-anal skin, where the resistance has forced the abscess into the ischiorectal areolar tissue. The abscess may even penetrate the levator swing to the supralevator or retrorectal space as indicated by both peri-anal and rectal bulging.

Rectal bulging into the ampulla in the absence of peri-anal induration or fluctuation indicates the comparatively rare submucus abscess.

Technic — Anesthesia is induced by pentothal sodium given intravenously. With the patient in the dorsosacral position, the large abscess is opened through a long, 2- to 3-inch peri-anal tangential incision over the height of the fluctuant mass. The surgeon's index finger then breaks up the loculi, while the other index finger is inserted into the rectal ampulla to palpate the levator floor. If bulging is found on palpation, the diaphragm is opened digitally or bluntly with curved forceps through the peri-anal wound. Injury to the rectal wall must be avoided. Tissue for biopsy and a culture of the pus is obtained for both routine and anerobic study. Administration of the antibotics or sulfanilamide is seldom necessary if adequate drainage is obtained and the patient's temperature quickly returns to normal.

FISTULECTOMY

Excision of the fistulous tract is an elective procedure. Hospitalization is planned by surgeon and patient after several weeks of recuperation. Sitz baths and regular examinations during the interim assure con-

3. Tucker, C. C. and Helwig, C. A.: Histopathology of the anal crypts, *Tr. Am. Proct. Soc.* 34: 47, 1933.

4. Young, H. M.: Ano-rectal fistula: historical background and modern treatment, *Ann. West Med. & Surg.* 2: 206, 1948.

tinued drainage and subsidence of the active infectious process. Anoscopic and proctosigmoidoscopic examinations are carried out routinely during this period and the causes of the fistula are determined. The presence of malignant growths, which are prevalent in the lower bowl, must be ruled out of the picture by these studies.[5]

The employment of low spinal or combined caudal and transacral block (second sacral foramina) anesthesia have definitely contributed to the success of fistulectomy. Under such sphincter-relaxing anesthesia, painstaking definitive surgical eradication of involved and scarred crypts, hemorrhoids and fistulous tracts is accomplished. This should not be attempted in the abscess stage. There is, however, one exception to this rule. When the comparatively rare submucus perirectal abscess is encountered, low spinal anesthesia is used and the abscess, bulging into the rectal ampulla, is opened with the actual (Post) cautery. With adequate rectal retraction, a longitudinal incision is made through the mucosa over the bulging mass, with the cautery extending it down to the involved crypt. Then, with sharp dissection, the involved crypt is excised and a racket-shaped area of adjacent peri-anal and anal canal epithelium is removed, affording adequate drainage to the outside. It may be necessary to sever the superficial external sphincter fibers at right angles to their course if they impede drainage.

Fistulous tracts or tunnels arise in anal crypts which constitute the primary orifice. Secondary orifices, of course, usually are external and peri-anal, but occasionally may be internal, opening through the rectal mucosa above the crypt line. Secondary orifices may also be multiple. The so-called horse-shoe fistula has its primary orifice in a posterior crypt and the tract or tracts swing laterally with secondary openings found in the anterior peri-anal area.[6]

Technic of Operation -- Adequate drainage and preservation of sphincter function are the two paramount surgical principles observed in operation of the anorectal area. An unroofing procedure clarifies the work at hand. The tract is first cannulated with a malleable probe from the secondary to primary orifice with the finger in rectum. Forceful entrance into the crypt should never be attempted.

Often, in a horse-shoe fistula, the outer curving tract may have to be first cannulated and laid open. Through a V-shaped area of excision, the apex of which is in the peri-anal skin, the anal epithelium over-lying the tract is excised. This is best accomplished by painstaking dissection with Hilton-type scissors. The anal epithelium is thus lifted from the external sphincter, carefully guarding each fiber. The limbs of the incisions are carried into the anal canal, passing the crypt line and on into the rectal mucosa. Flanking anal and internal hemorrhoids are included in this flap, which is raised from the sphincter.

Momentarily, the cannulated fistula is ignored. The unroofing process is completed by ligating the base of the mobilized mucosa with linen sutures, utilizing the two-needle technique in order not to purse-string the mucosal stump just above the excised crypt area.

Removal of a wide, racket-shaped portion of peri-anal and anal skin and redundant hemorrhoid-bearing mucosa from the area secures ade-

5. Scarborough, Robt. A.: Primary carcinoma of an anal gland, *Tr. Am. Proct. Soc.* 42: 172, 1941.

6. Nesselrod, J. P.: *Proctology in General Practice*, Philadelphia, W. B. Saunders Co., 1950.

quate drainage of the ano-rectal wound. The sphincter fibers are now plainly visible and the fistulous tract is lifted on the probe. The supervening muscle fibers of the sphincter are sharply severed at right-angles to their course. When encountered, the tough, scarred sheath of the tract can often be shelled-out en masse encircling the probe. The crypt should also be carefully excised at the distal end of the probe. A clean base of the wound is secured by thorough currettage. The blunt, cut ends of the sphincter should now lie in close juxtaposition. A final clean-up of the area with the crypt hook and scalpel insures against damming the drainage ditch to the outside.

Hemorrhoids or redundant tissue in the opposite or contra-lateral sector of the ano-rectum may be excised through a similar unroofing resection. Here, too, the superficial external sphincter fibers are often severed at right angles to their course in order to allow for closer approximation of the cut muscle at the site of the fistulectomy. A rubber dam drain, 1 inch wide by 6 inches long, wrapped with several thicknesses of oxycel gauze, is placed in the anal canal and a fluffed pressure dressing is applied.

POSTOPERATIVE CARE

Sitz baths and regular examination of the drainage tracts are extremely important in the immediate postoperative stage. A cotton applicator may be drawn along their courses to break up synechiae. Careful digital examination will prevent reformation of tunnels or any tendency towards anal stenosis.

Anterior anal fistulous tracts in female patients often present a special problem because the transverse perineal support is not stable. In such cases a plastic or transposition procedure may be possible. Mobilized anterior rectal mucosa may be brought down and tacked to the outer sphincter fibers in order to cover the primary orifice after the crypt is excised. Wide dranage is then affected.

Finally, a word about the string seton. Its present day use is seldom necessary or advisable unless nearby double tracts through the sphincter are present.

The gauze pack, formerly used to fill the tract, is not advised because it separates the sphincter ends and causes seepage and partial incontinence.

Tuberculous fistulae can be treated and healed if the principles mentioned and general supportive care are carefully followed. The external drainage tracts should be very radical in these cases.

Peri-anal abscesses in cases of ulcerative colitis should be widely opened. Definitive surgical operation for the removal of fistulous tracts in these patients should be planned during periods of remission of the diarrhea.

SMALLPOX

In 1950 only 41 cases were reported in U.S. For the decade 1920 to 1929 the total of reported smallpox cases in U.S. amounted to more than 500,000. The greatest number of small pox cases in 1950 was reported by Kansas (7), followed by Kentucky (6) and Oklahoma (5). 30 states did not report a single case of smallpox in 1950 while in 1940 only 12 states were free from the disease and in 1930 only 7.

The Problem of Impotence

Impotence, either of psychic or organic origin, in many instances may be treated by the family physician.

EDWARD PODOLSKY, M.D., *Brooklyn, New York*

Impotence is the loss of ability to effect and maintain an erection of the male sex organ, the penis. Sexual ability is based on two things, sexual desire and the ability to obtain and maintain sufficient erection. If desire is absent, little can be done about the situation. Erection is maintained largely by the organs of the posterior urethra, particularly the prostate and the seminal vesicles. When these organs are emptied of their secretion erection is not possible.

In general, impotence is divided into two great groups: Organic impotence and psychic impotence. Organic impotence refers to a condition in which the ailment is due to some organic or structural condition in the body which is responsible for the disease. Psychic impotence is the result of some severe mental or emotional disturbance.

ORGANIC IMPOTENCE

Organic impotence has as its origin some disorder which interferes with the normal erection of the penis. The man may feel normal in all respects with the exception that his sexual power is below par. Loss of sexual strength may come on suddenly, but more often it is a gradual and drawn-out process.

CAUSES

Obviously, there are many causes of organic impotence. Any disease or disorder which affects the sex organs may result in this disability. Venereal infections may play a prominent role in this connection. Inflammation of the internal organs of the genito-urinary system, such as the prostate or seminal vesicles will result in a loss of sex power. The prostate may become soft, boggy, enlarged, indurated, and exert a harmful effect on the ability to perform the sex act.

Deficiency in the secretion of the endocrine glands (particularly of the gonads or sex glands) quite often results in impotence. New growths in the region of the genitals may also have a deleterious effect. Diseases of the nerves intimately connected with the sexual function may result in impotence. The excessive use of

drugs, alcohol and narcotics has often resulted in lessened sexual power.

In general, it is well to be aware of the fact that certain other important factors may also be implicated in the causation of decreased sexual power in the husband. Among these may be too frequent sexual activity, general fatigue and debility, too much use of mechanical contraceptive devices, coitus interruptus, and various abnormal sexual practices.

PSYCHIC IMPOTENCE

Many difficulties of the recently married couple arise from incomplete information on the technique of sex relations. Disproportion of the sex organs of the male and female, resistant hymen, improper lubrication, are all causes which may result in lessened sex power. These may seem like rather negligible factors, but their very neglect may lead to complete impotence in the man and frigidity in the woman.

Quite often, what one might consider a sexual practice of little or no consequence may lead to impotence. Coitus interruptus is a rather common practice. Quite a few husbands regard this practice too lightly. But, is it always harmless? Far from it. Coitus interruptus may bring on an inflammation of the seminal vesicles, which not infrequently, is the cause of sexual weakness.

When a man's health in general undergoes severe changes, it is likely also to result in a diminution of his sexual power. Low blood pressure may often result in poor erection and inability to perform the act. Serious diseases of the blood, the heart, the kidneys and other vital organs may result in a decreased sexual urge.

In addition to the conditions described above, impotence may be caused by mental, emotional and psychic upsets of various sorts. In general, there are several rather well-defined causes of what is termed pyschic impotence.

The fear of impregnating the wife when pregnancy is not wanted is often a drawback and a cause of psychic impotence. Fear destroys sex desire and potency in the man. Sometimes this fear is so great that the power of erection is lost. Lack of cleanliness on the part of the wife may also act as a means of causing impotence. Certain strong emotions, such as anger, disgust, fear, may temporarily upset the power to perform the sex act. Sometimes impotence may be the result of general insecurity and anxiety, engendered by other situations in life, such as financial losses, occupational strain and worry. There are other causes, however, in which the difficulty may be rooted much more deeply in the personality, and such factors as abnormal sexual desires, fear of venereal infection and a feeling of sexual inadequacy may actually result in impotence.

Cases of impotence have been reported which were caused by hatred of women, homosexuality, masturbation and sadism. Psychiatrists under whose supervision these cases come give us the following facts regarding psychic impotence:

1. An individual's sexual potency varies with the love he bears for his wife. Lack of love, no matter what the cause may be, destroys his power to perform the sexual act.

2. Extreme fear and anxiety will often destroy sexual power.

3. Fear of the consequences of masturbation, such as insanity and crippled children, will often render a man impotent. There is no doubt that this fear is entirely unfounded, but there are still some books and parents who have weird notions which

they instill in young boys' minds with dire later results.

4. Homosexuality and other abnormal sex desires often render a man incapable of performing the normal sexual act.

5. Disturbances in organism may be manifested by reduction in intensity, and result in impotence through worry and other strong mental and emotional upsets.

GRADATIONS OF IMPOTENCY

There are various degrees and gradations of impotency. These may be listed as follows:

1. Potent, but pleasure is lacking during sexual intercourse.

2. Potent, but coitus is indulged in under protest.

3. Interested in sexual intercourse but cannot always have an erection when desired.

4. Poor or only partial erection.

5. Premature ejaculation.

6. Complete impotence but still has interest in sexual relations.

7. Complete impotence with no interest in sexual relations.

Let us consider each of the above headings separately:

1. *Potent but no pleasure is experienced in coitus.* These men are able to have an erection when desired, and yet there is always something lacking in the achievement of the anticipated pleasure. These men like to talk about sex but do not derive any pleasure from the sex act itself. Such men never become satisfactorily adjusted in marriage.

2. *Potent but coitus is performed under protest.* These men have little difficulty in getting an erection and having sex relations. However, they are under the impression that coitus is harmful and deprives them of strength and energy. They always feel tired, weak and exhausted after the sex act, and for this reason sex relations are indulged in at infrequent intervals.

3. *Interested in coitus but cannot always have an erection when desired.* In this group are the men who find sexual intercourse desirable, but when the time comes around for the sex act they cannot achieve an erection.

4. *Partial erection.* These men are interested and eager for sexual relations, but they are able to have only a partial erection which is so weak that penetration cannot be achieved.

5. *Premature ejaculation.* In this group ejaculation takes place before it is supposed to. There is therefore a lack of sexual gratification in the woman.

6. *Complete impotence with interest in sexual relations.* In this group erection is lost but the man is still interested in sex. These men are more amenable to treatment than the last group.

7. *Complete impotence with no interest in coitus.* This type of man is completely impotent and has no interest in sex whatsoever. Such men suffer from very serious nervous ailments and are very difficult to treat.

SUMMARY

Impotence may be divided into two groups, namely, organic impotence and psychic impotence.

Organic impotence is caused by a disorder which interferes with normal erection. Correction of the underlying disorder may restore sexual power.

Psychic impotence is much more difficult to treat because the underlying factors must be ferreted out, usually by a trained psychiatrist, before sexual power is gained or restored. Occasionally, reassurance may be all that is necessary.

Carbon Monoxide Poisoning

A review of the variations of clinical manifestations of carbon monoxide poisoning, cause of many suicides and fatal accidents.

LUDWIG TELEKY, M.D., *New York, New York*

At present, about 2 per cent of fatal accidents in the United States are due to carbon monoxide poisoning, while about 50 per cent are caused by other kinds of gas. Ten per cent of all suicides in 1948 were due to carbon monoxide. Of these 1,894 cases, 625 suicides and 254 fatal accidents were caused by motor gas. The ways in which such suicides or accidents occur differ widely and thus, the clinical syndome also varies.

As the most common clinical picture of carbon monoxide poisoning is well known, only the many variations of the clinical manifestations shall be discussed here.

CLINICAL SIGNS

When a person inhales gas, he may succumb within 15 or 30 minutes. If he is found unconscious, even though his condition is critical, with respiration and pulse almost absent, he may be revived by means of artificial respiration and administration of oxygen even after 30 minutes has elapsed. As a rule, he will recover in two or three days.

When gas infiltrates slowly into a room, the occupants may not become aware of the danger. One may find an aged person, peacefully sitting in the kitchen, killed by gas. If found alive, the prognosis in such a case of slow poisoning generally is unfavorable.

I once examined a strongly built woman about 30 years of age, in her bed in the bedroom. She had not been seen for 36 hours. The tap of the gaslight was slightly open. The patient was unconscious, although the heart action and respiration were satisfactory. She remained in coma for four days, and then died. Examination at autopsy revealed the characteristic softening of the pallidum, caused by malnutrition of the ganglion cells due to saturation of the blood with carbon monoxide.

The prognosis in cases of carbon monoxide poisoning caused by a large quantity of carbon monoxide inhaled within a short time is better than in those caused by prolonged inhalation of small amounts of gas.

Peculiar cases have been ob-

served. In acute poisoning, bodies have been found in positions as if they were still alive. The victims had been overcome by a catatonic stupor, quickly followed by death and rigor mortis. This was found in the case of miners in the mine disaster of Courrieres, France, in 1906, and in soldiers in the land mine war of World War I.

SYMPTOMS

The first stage of carbon monoxide poisoning presents clinical symptoms of animation, psychomotor hyperactivity, and spells of laughing. In a bus in which carbon monoxide penetrated, the passengers first became very gay and noisy, followed by tranquility. Finally, many persons became unconscious and one died.

In other cases, there may be inclinition to violence. For instance, a signalman, in whose house gas entered, left to give the train signal, and after returning he killed his wife and injured her sister. A ship's captain through whose cabin carbon monoxide had diffused, shot the cabin boy who tried to wake him. In a case in France, a husband and his brother were found dead in a house; the wife appeared mentally disturbed. It was believed that she had killed both men and she was sentenced to hard labor. Several months later an unclarified death occurred in the same house. Carbon monoxide was detected as the cause, the source being a defective oven. The woman's sentence was reversed. A story was published in newspapers of carbon monoxide poisoning in a family. The children died and the mother was found mentally disturbed; she had amnesia for the immediate past in which the poisoning had occurred and was unwilling to believe the death of her children.

COMPLICATIONS

When both respiration and pulse in cases of carbon monoxide poisoning remain satisfactory and when consciousness is regained within the first few days after poisoning, transient disorders of the cardiovascular system, hearing, the peripheral nervous system (neuritis), and psychic disturbances may appear. In about 5 to 10 per cent of cases, fatal pneumonia develops.

More important are late or permanent sequelae, especially after prolonged poisoning. Such sequelae have been recorded in approximately 5 per cent of severe cases and may develop immediately after poisoning or several weeks later. There may be a variety of nervous or psychic disturbances.

French authors list a number of possible sequelae, among them disorders of vision, hearing, emotional reactions, hemiplegia, convulsive disorders, and Parkinsonism. Late sequelae are not too rare. I have seen among ninety-two surviving, severely poisoned patients, five with permanent cerebral damage.

DIAGNOSIS

The diagnosis is not always easy and depends mainlv on the clarification of the circumstances and examination of the blood. Difficulties and uncertainties may be the environmental conditions.

I saw the case of a blacksmith who had worked for 10 years on the same hearth. In a night with abnormally low temperature and strong winds, the exhaust pipe failed to operate properly and the blacksmith was killed after working at the hearth not longer than 20 minutes. Bathroom accidents may have the same effect. As to the objective signs, it is generally pointed out in text books that lips, ears, and especially cadaveric spots display a bright red color. In some cases this coloring may be found, but frequent-

ly, I have not detected this discoloration. Binet and Conte stated that in 126 cases of carbon monoxide poisoning, they saw this discoloration only two or three times. Therefore, in every unclear case of death occurring in factories, a careful laboratory examination of the blood should be carried out. It should be stressed, however, that evidence can be obtained only when the blood has been taken within the first few hours after death.

TREATMENT

When a carbon monoxide poisoned person is found, resuscitation should be carried out immediately. If the patient is breathing well, whether unconscious or not, administration of oxygen is indicated. Henderson and Haggard, in 1920, recommended 'Carbogen' which is a mixture of 92 per cent oxygen and 7 per cent carbon dioxide. I always felt that this recommendation rested only on theoretical considerations. Recently, Schwerma, Ivy and associates showed that this mixture is not superior to pure oxygen.

If the poisoned victim does not breathe regularly or is not breathing, artificial respiration should be started. Under all circumstances, artificial respiration should be continued until the patient breathes spontaneously and regularly or until death is beyond doubt.

Instead of manual artificial respiration, apparatus can be used both for artificial respiration and for oxygen inhalation. These apparatus are available at all first aid stations. During artificial respiration and administration of oxygen, blood and cardiac stimulants may be given.

In my opinion, rigor mortis is the only one reliable sign of death in these cases. It begins about an hour after death, first may be observed on the feet and may be recognized in attempting to flex the ankle joint. If resistance is encountered, rigor mortis has set in in the gastrocnemius muscle.

RABIES

The incidence of neuroparalytic accidents complicating application of rabies vaccine has been variously reported by American authors as ranging from 1 in 280 to 1 in 8,287 treated patients. Worldwide statistics, on the other hand, which were reported by M. Greenwood (Tenth Report on Data of Anti-Rabic Treatments Supplied by Pasteur Institutes. Publ. Health Organ, League of Nations, 12:301, 1945-46) estimate the incidence rate at 1 in 5,814 in a series of 1,290,758 treated patients with a mortality rate of 25%. In the state of Michigan approximately 6,000 patients received 84,122 doses of rabies vaccine from July 1, 1945 to March 31, 1949. During this period 12 cases of reactions, including 4 cases of neuroparalytic accidents with one death were reported to the Michigan Dept. of Health. (F. R. Latimer; J. E. Webster and E. S. Gurdjian. Arch. Neurol & Psychiat., 1:16, January 1951).

The Alopecias

A review of the factors causing temporary or permanent baldness and methods of treatment.

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It is advisable to distinguish two main groups of processes which lead to alopecia—(1) those which end in permanent alopecia because of atrophy of the germinative epithelium of the hair and (2) those in which the hair loss is not permanent because damage to the germinative epithelium is transitorial.

PERMANENT ALOPECIA
PREMATURE MALE BALDNESS

In this group by far the most common disease process is premature male baldness. Over forty per cent of the adult white male population shows evidence of this type of hair loss.

A physiological sex difference between the scalp hair of males and females becomes manifest at puberty. Whereas throughout childhood the anterior hairline is a rounded one, soon after the onset of puberty boys develop a triangular incisure in this line in both temperal regions. This "calvities frontalis adolescentium" is so characteristic for the adolescent male that it can be regarded as a secondary sex character. In delayed puberty its absence is as conspicuous as is the absence of beard development and greatly contributes to a "baby face" appearance. Reversely, in women with some masculine features such as deep voice, hypertrichosis, etc., rudimentary frontal calvities can sometimes be observed.

The pathological male baldness starts in the majority of cases shortly after the physiological frontal calvities has developed but may remain undiscovered for a long time because of the great density of hair on the scalp throughout childhood. The loss of hair has a characteristic symmetrical pattern. It starts on the vertex and in the two temporal incisures at about the same time. First it can be recognized only by a more profuse shedding of hair from these areas and only later by actual scantiness of the hair. The follicular germinative epithelium undergoes an

extremely slow and gradual withering. These follicles may produce hair for many years after this process has set in but as it progresses the subsequent generations of hair become thinner and shorter lived.

The balding process extends from the vertex frontally and from the temporal incisures posteriorly. The well known end result is complete baldness of the frontal and parietal regions while a relatively well preserved wreath or crown of hair persists in the temporal and posterior occipital areas. The course of this "Hippocratic baldness" including its rate, duration and ultimate extent are quite variable. Frequently the balding process spontaneously ceases after a number of years or there may be several alternating periods of active progression and quiescence. Some men become almost entirely bald in their early twenties while others in spite of showing definite signs of the balding process such as recession of the frontal hairline and/or a bald spot on the vertex, may retain substantial amounts of hair for numbers of years. Thus, it is difficult to prognosticate about the final outcome of this balding process in any of its stages. The only good prognostic hint available is the severity of the genetic background for baldness in the family.

Early male baldness in most cases is associated with clinically manifest seborrheic dermatitis of the scalp. This is a mild inflammatory process associated with scaling ("dandruff") and moderate itching. That this is an inflammatory process can sometimes only be shown histologically but often it may be manifest clinically in the form of reddening of the scalp. Because of this association with seborrheic dermatitis, early male baldness has been called alopecia seborrheica. However, it is obvious that the seborrheic dermatitis cannot be the sole cause of the balding process because a great number of men and women suffer from severe seborrheic dermatitis of the scalp without getting bald. Moreover, seborrheic dermatitis on other parts of the body does not lead to atrophy of the follicular germinative epithelium and hair papillae. Also, from a therapeutic viewpoint, one can control the seborrheic dermatitis fairly successfully and yet not influence the balding process.

It has been claimed that successful treatment of the seborrheic dermatitis can retard or arrest the hair loss and certainly no harm can result from such treatment. Shampooing once weekly with tincture of green soap U.S.P. and massaging of tiny amounts of an ointment containing sulfur and salicylic acid into the scalp twice weekly (once after shampooing when the hair is dry and then again in the middle of the week) are commonly recommended for this purpose. For seborrheic dermatitis of average severity we use three per cent precipitated sulfur and two per cent salicylic acid in unguentum aquae rosae. The concentration of sulfur can be varied according to need. In cases of irritable scalps one to two per cent sulfur is preferable whereas in cases associated with sever aleic seborrhea the sulfur concentration may be as high as ten percent. It has been our own impression that this treatment in some cases slows down the balding process. Certainly in the majority of cases it quite satisfactorily relieves the seborrheic dermatitis.

ETIOLOGY

Aristotle is credited with observing that babies, women, and eunuchs never become bald. Our knowledge about the etiology of early male baldness has not progressed much further since then. Three definite

etiologic factors can be recognized. These are heredity, age, and male sex hormone. Nothing can be done about the first two factors and elimination of the latter is scarcely to be desired Hamilton has observed that eunuchs, who never develop premature alopecia naturally, showed signs of developing baldness when given androgen therapy if this trait was prevalent in their families. Cessation of androgen in these individuals stopped the progression of the alopecia but did not cause regrowth of hair in areas already bald. Of course no regrowth of hair from atrophied follicles could be expected.

Although the mode of inheritance is not entirely clear, the pattern of early male baldness in space and time is frequently carried through the maternal side of the family, the females being conductors of the trait without disease as in hemophilia. In other families however, the transmittance can be traced to the paternal ascendance. Osborn considers the inheritance to be sex-limited, being dominant in men and recessive in women. This type of alopecia practically never occurs in women but on rare occasions it may be seen to a mild degree. Excessive androgen production is frequently suspected in these cases but often no endocrine disturbance can be demonstrated. The hereditary factor may be prominent in these cases.

From time to time etiologic theories for early male baldness have been proposed centering about circulatory disturbances in the scalp. The causes for such disturbances have been claimed as anything from tight hat bands to chronic tension of the scalp either mechanical or from psychogenic muscular strain. No disturbance of scalp circulation however, has ever been actually demonstrated and the selectivity of the atrophy for the papillary capillaries of the hair argues against impaired circulation being at fault. Also it is well known that the balding process is connected with sebaceous gland hypertrophy, a process which hardly can be reconciled with impaired circulation or tissue anoxia.

Patterned male baldness entirely similar to that in man occurs in the higher apes. Tight hats obviously play no role here and who can evaluate the psychic stresses under which a balding jungle simian lives?

All other processes which result in diffuse or circumscribed permanent baldness are of much lesser significance and are more of dermatological than general interest. Among these, congenital rudimentary development of hair or even complete absence of hair (atrichia) is a rare familial anomaly. Some of these cases are associated with hypoplasia of the teeth, sweat glands, and nails (hereditary ectodermal dysplasia).

CICATRICIAL ALOPECIAS

The circumscribed cicatricial alopecias may have a great number of causes besides actual trauma followed by scarring. Any skin disease leading to atrophy or scar formation can cause this type of hair loss. The chronic discoid type of lupus erythematodes is a well known such disease. Besides the irregularly shaped blad patches in this disease, the skin characteristically shows erythema, infiltration and follicular plugging during the active stages. Later atrophy, scaling, dilated pores and sometimes telangiectasia become evident. Laboratory signs such as borderline leukopenia, elevation of the sedimentation rate and increased plasma globulins are often present even in this chronic discoid type of lupus erythematodes. Intravenous gold therapy is the treat-

ment of choice if no signs of dissemination are present.

Circumscribed scleroderma is also a relatively frequent cause of alopecia. Usually a sagital, narrow, paramedian band of rigid atrophy and hair loss gradually develops over the frontal portion of the scalp (scleroderma en coup de sabre). There is no effective therapy.

Noduloulcerative syphilids, gummata, cutaneous tuberculosis, sarcoidosis, leprosy, favus, and deep mycoses are other well known diseases commonly followed by a cicatricial type of circumscribed alopecia. Gangrenous herpes zoster, neoplasms, keloidal acne and a large number of rare dermatologic entities of unknown etiology such as pseudopelade and folliculitis decalvans are still other causes of circumscribed cicatricial alopecia. Treatment where possible should be directed against the primary disease during its active stages.

TEMPORARY ALOPECIA

Temporary alopecia may occur in infants during the first few months of life when the fetal lanugo on the scalp is shed and terminal hair appears. In the majority of cases this generation change occurs before birth. The degree and duration of alopecia produced by this process is quite variable but by one year of age it is always gone.

"TOXIC" DEFLUVIUM

The most classical example of temporary hair loss without permanent damage to the hair papilla or germinative epithelium is the occasional profuse defluvium observed almost exactly three months after the occurrence of some febrile illnesses. This type of hair loss is called symptomatic, toxic, or postinfectious defluvium. This defluvium has a stormy course insofar as a frighteningly great numbers of hairs loosen and can be pulled out with greatest ease. At each shampooing many hundred of hairs are lost. The club of these hairs is thin. Within a few weeks the patient may lose one third to two thirds of all the scalp hair. Any severe illness accompanied by high fever such as typhoid fever, pneumonia, influenza, erysipelas, and scarlet fever may be followed by such a diffuse hair loss three months later. Fortunately, almost without exception, the hair regrows to full restitution within a year after these post-febrile alopecias appear. In some cases, however, particularly after typhoid fever, regrowth is sometimes unsatisfactory. Similar symptomatic alopecia occurs not uncommonly following pregnancy or abortion. Also, in early secondary syphilis a toxic type of alopecia as described above sometimes occurs. In contrast to other kinds of post-infectious defluvium this latter type also involves loss of axillary and pubic hair.

In cases of profuse loss of hair with sudden onset it is of great importance in order to insure the diagnosis to inquire about antecedent illnesses which may have been forgotten by the patient (e.g. influenza lasting just a few days). Symptomatic alopecia is often associated with transverse white lines and with corrugations of the nails called Beau's lines.

ALOPECIA AREATA

Alopecia areata, a fairly common disease of unknown etiology, consists of sharply circumscribed patches of sudden complete hair loss. It may involve any part of the scalp or any other portion of the body hair. It occurs at any age from infancy to old age and in both sexes with equal frequency. There are usually no accompanying symptoms. When noticed, the bald patches are two to three centimeters in diameter.

These commonly enlarge in circular fashion by peripheral extension and may become confluent with other lesions. During active phases the hairs at the periphery of the patches are loose and show narrowing near their lower ends ("exclamation-point" hairs). The course of the disease is quite unpredictable. At times only one or two small patches will be present for a few months and then disappear. At other times new lesions will continue to appear and enlarge until the entire scalp hair is lost (alopecia totalis) or even further until not a single hair including eyelashes and eyebrows remains on the body (alopecia universalis).

The skin of the bald areas remains entirely normal and the follicles are usually not atrophic. In the milder forms regrowth of hair generally occurs in six months to one year. The new hairs at first are often non-pigmented but later the normal color returns. There is, however, a very marked tendency towards recurrences in the same individual sometimes even decades after the initial attack.

SEVERE ALOPECIA AREATA

Severe alopecia areata and the totalis and universalis types are more often seen where the initial attack occurs prior to puberty. Dystrophic nail changes may accompany these more severe types. In these severe cases the hair loss tends to be permanent. The prognosis however is not entirely hopeless since hair has on occasion suddenly regrown after even five or ten years of absence. Atrophy of the involved hair follicles if it occurs takes many years to develop. The disease is not contagious.

Theories about etiology have been made and varied. Toxic, endocrine, infectious, psychogenic and neurogenic causes and combinations of these have all been proposed but none conclusively proved. The afflicted individuals in general are entirely healthy except for the hair loss. As pointed out by Walker and Rothman, endocrine factors may play a modifying role in the disease for the following reasons: (1) The course of alopecia areata is more severe prepubertally. (2) Some cases begin simultaneously with thyrotoxicosis. (3) Several cases of the severe totalis variety have recovered completely only during pregnancy and lactation and then relapsed afterwards; and (4) recent experiments with cortisone therapy suggest that it may lead to at least temporary regrowth of hair.

TREATMENT

Local therapy to date has been of questionable value. However, ultraviolet light irradiations and mildly rubefacient alcoholic lotions are commonly prescribed.

Certain metals and drugs as thallium, tin, and arsenic can cause a diffuse toxic alopecia. The hair loss following exposure to X-rays or other penetrating ionizing radiations also belongs in this category of alopecias. The prognosis for regrowth in these types of alopecia depends on whether the toxic factor can be eliminated and to what extent the follicles have been permanently damaged.

Toxic defluvium, alopecia areata, and temporary X-ray epilation (as practiced in the treatment of tinea capitis) seem to have in common that they loosen the hair from its base without seriously damaging the germinative epithelium.

BALDNESS SUBSEQUENT TO INFLAMMATORY PROCESSES

Temporary hair loss also occurs following a variety of local inflammatory processes. The most important example here is the usual type of patchy syphilitic alopecia in which scattered irregular small spots display conspicuous scantiness of hair

but not complete baldness. There is a predilection of these spots for the occipital region and the eyebrows. This type of syphilitic alopecia appears as a late secondary manifestation of the disease and is frequently observed together with a follicular syphilid or with leucoderma colli. It is more common in women and is often associated with early neurosyphilis. The sites of involvement are presumably at points where syphilitic papules were present. No scarring results and regrowth of hair occurs within a year. More prompt regrowth follows effective antisyphilitic therapy.

Local spotty alopecia of the eyebrows of a similar type is seen in association with lepromatous or leukemic infiltrations.

MISCELLANEOUS CAUSES OF SCANTY HAIR

Malnutrition and chronic debilitating diseases such as tuberculosis and cancer may be accompanied by a slowly developing diffuse partial alopecia. Similarly hypothyroidism and hypopituitarism can be associated with general thinning of hair.

Of the mechanical or facticial alopecias the most common is that seen in infants over the occipital area as a result of constant lying on the back and rubbing against the bed clothes. Another common type is seen in neurodermatitis where the eyebrows may literally be erased as a result of constant rubbing because of the intensely itching skin disorder.

Excessive tension placed on the hair usually in an effort to straighten kinky hair or to braid very short hair can also cause mechanical alopecia.

Trichotillomania represents a compulsive urge to pluck, break off or otherwise remove the hair. The resulting hair loss may present quite bizarre patterns. This type of alopecia may be merely a mild habit neurosis or may be part of a more severe neurosis or psychosis.

HAIR SHAFT DISEASE

This paper does not deal with processes in which the hair shaft merely breaks and where there is not complete loss of hair from the follicles. The most common of such hair shaft diseases is ringworm of the scalp (tinea capitis) which occurs almost exclusively in children and in which fungi actually invade the hairs. Other less common hair shaft distrubances that may lead to scanty appearing hair include monilethrix in which there is a periodic thinning of the hair shaft with a tendency for breaks to occur in the thinned areas; trichorrhexis nodosa in which the hair shaft shows nodular brush-like areas of longitudinal fragmentation where rupture readily occurs; and fragilitas crinium which is characterized by longitudinal splitting and unusual brittleness of the hair.

HEART DISEASE

The Vancouver Unit of the Division of Tuberculosis Control of British Columbia from December 1948 through July 1949, checked all microfilms taken for signs of heart pathology. Where such pathology was found, a larger x-ray picture and an EKG were done. From a total of 7,093 microfilms, 158 cases displayed cardio-vascular abnormalities; 33 of these individuals were unaware of existing heart disease, and many others did not associate their symptoms with a heart ailment.

Tuberculosis of the Female Genitalia

Early diagnosis, use of antibiotics, and surgical procedures are employed in eradication of this condition.

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Fifty years ago, genital tuberculosis was an entity of great importance in gynecologic practice. At present, it is a disease of lesser interest. Nevertheless, the use of antibiotics and the knowledge obtained through studies of sterility have made the subject worthy of discussion.

ETIOLOGY

Tuberculosis of the pelvic organs is usually secondary to primary foci of infection elsewhere in the body, although occasionally it may be primary. Cases referred to as primary pelvic tuberculosis are those cases in which a careful history and exhaustive roentgenographic and laboratory studies fail to reveal any other site of infection. It is well known that tuberculosis of the female genitalia is usually hematogenous in origin, except in cases of generalized tuberculous peritonitis. The ascending infection is rarely encountered.

The Fallopian tubes seem to be affected more often than the endometrium or the cervix. (Recently, several European gynecologists have questioned this fact because of the number of cases of tuberculous endometritis found in which the tubes were patent). It is estimated that about 5 per cent of diseased tubes are due to tubercle bacilli. The diagnosis of tuberculous salpingitis is seldom made before operation and even then it is remarkable how often it is unrecognized.

SYMPTOMS

The most common complaints are pain and menstrual disturbances. Oligomenorrhea and amenorrhea occur more often than emenorrhagia or metrorrhagia, especially if the pelvic tuberculosis is secondary to an active pulmonary focus. Sterility is common in such patients and, as in other types of salpingitis, leukorrhea is present. Frequently, the temperature is slightly elevated. If a tube-ovarian abscess is present, it may be more elevated.

DIAGNOSIS

Pelvic examination following a careful history is very important. Whenever a patient complains of

pain, menstrual irregularities or sterility, and if the patient or her immediate contacts have a previous history of tuberculosis, tuberculosis of the pelvic organs should be suspected. Also, any previous bone infection should be investigated. Tuberculous salpingitis should always be considered when a diagnosis of salpingitis is made if the hymen is intact. Leukopenia is common in tuberculous salpingitis except in those cases in which a tubo-ovarian abscess is present.

Dilatation and curettage aids in the diagnosis of tuberculous salpingitis, and may be carried out except in cases of acute or subacute salpingitis. In cases of ascites with an adnexal mass, in which an ovarian malignant tumor has been ruled out, it is worthwhile to remember that the younger the patient the greater the chance of pelvic tuberculosis, as most cases occur between the ages of 20 and 40 years. Also, whenever salpingitis does not respond to treatment with antibiotics within 10 days, exclusive of streptomycin, it is probable that tuberculous salpingitis is present. In some instances, the pain and temperature will respond to treatment, but the pelvic findings will remain the same. Tuberculosis of the cervix, which is rare, can be diagnosed by biopsy. Examination of cultures of vaginal secretions and inoculation of guinea pigs will help in the diagnosis of pelvic tuberculosis.

DIFFERENTIAL DIAGNOSIS

Tuberculous salpingitis must be distinguished from gonorrheal or streptococcal infections. Pain is usually more severe in gonorrheal salpingitis and is frequently accompanied by cervicitis, bartholinitis, or infection of Skene's glands. A temperature of 101°F. is frequently encountered in gonorrheal and streptococcal salpingitis. These two forms of salpingitis readily respond to chemotherapy and antibiotics they are not encountered as frequently as they were 15 years ago.

In the so-called "frozen pelvis," endometrial biopsy will aid in the differential diagnosis of carcinoma.

In those cases in which a few nodules are found in the cul-de-sac and along the sacro-uterine ligaments, the differential diagnosis with endometriosis must be made. In endometriosis, the pain usually decreases for a few days after menstruation. The condition can be improved by preventing ovulation through the administration of hormones.

GROSS DIAGNOSIS

If diagnosis has not been made prior to operation, it is necessary to recognize the nature of the disease grossly so that the proper procedure can be performed.

It is well to keep the following in mind:

1. The fimbriated ends of the tubes are usually open in tuberculous salpingitis, while they are closed and inverted in gonorrheal or streptococcal salpingitis.
2. Usually, the ovarian involvement is only peri-oophoritis.
3. The adhesions are more severe in tuberculosis and endometriosis than in other forms of salpingitis.
4. The serosa of the tubes, colon and pelvic organs should be carefully examined for the presence of tubercles.
5. The mucosa of the tubes is attacked first by tubercle bacilli except when the tubal infection is secondary to a tuberculous peritonitis.

TREATMENT

If tuberculosis is recognized at the time of operation, the least radical

operation that should be performed is bilateral salpingectomy. Usually, hysterectomy and bilateral salpingectomy are advisable. Preservation of the ovaries, if they are not diseased, should be attempted in younger patients. The cervix may be spared in cases in which adhesions make its removal a difficult procedure. If extension of the disease is marked, or if the patient is approaching the age of menopause, a more radical procedure should be performed.

Streptomycin should be administered in all cases diagnosed as tuberculosis, especially in tuberculous endometritis and in tuberculosis of the cervix. In cases of tuberculous salpingitis, streptomycin should be given before and after operation in doses of 2 Gm. daily for at least 6 to 8 weeks.

Roentgen therapy continues to be the treatment of choice of many gynecologists. The results obtained are excellent, especially in cases of the "frozen pelvis". The dosage used is much smaller than that used for malignant tumors, usually ⅛ to ½ of the tumor dose of 5 to 50 percent of the E S D.

Pneumoperitoneum may also be employed, particularly if a culdoscope is used as an aid in the diagnosis of pelvic disease. If tuberculosis is not recognized at the time of operation but diagnosed later and confirmed by the pathologist, roentgen therapy should be employed and streptomycin given. Further operation is not advised.

Periodic examination should be carried out in all cases of tuberculosis of the female genitalia for further evidence of the disease.

Isonicotinic Acid Hydrazide and Tuberculosis -An Evaluation

It is still too early for a definitive clinical assessment of the value of nicotinic acid hydrozide as an active antituberculosis agent in man. One or two facts are beginning to emerge, however, and have been assessed by Dr. William A. R. Thompson in the August, 1952, issue of *The Practitioner*. First of all, there can be no doubt about this drug being an active antituberculosis agent, although it is equally clear by now that it is inferior in this respect to streptomycin It may perhaps prove most valuable as an adjuvant to the latter antibiotic, possibly replacing PAS, or when used in conjunction with both streptomycin and PAS.

These possibilities are strongly suggested by evidence obtained in clinical trials performed on some 125 patients. It thus was observed that after four months of treatment with isonicotinic acid hydrazide, the average gain in body weight was 2.9 lb.; similar treatment with this drug plus streptomycin produced an average weight gain of 6.4 lb. Increased appetite and the sensation of euphoria are two additional striking effects induced by the drug. They are not necessarily accompanied, however, by a corresponding improvement in the sputum or the radiologic findings in the lungs. Still another notable property is the ease and speed with which the drug penetrates to all parts of the body, including the cerebrospinal fluid. This facility to breech the meningeal barrier suggests the possible value of this drug

(Continued on page 418)

Diagnosis and Treatment of Thrombo-Angiitis Obliterans

Early diagnosis of this disease, plus proper management, prevents amputation in numerous cases.

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Knowledge of the pathologic process underlying thrombo-angitis obliterans is inadequate. Although the pathologic picture of thrombo-angiitis obliterans is well known, it is unfortunate that so few cases are encountered early enough, or that are sufficiently advanced at an early stage, for the pathologist to obtain material for histologic study.

PATHOLOGY

Occasionally, portions of an amputated extremity have revealed changes in the arteries not occluded by thrombi which might be considered incipient thrombo-angiitis obliterans. These changes are minimal proliferation of the intimal cells, with small collections of lymphocytes in isolated portions of the intima. In the adventitia, lymphocytes are clamped about the vasa vasorum. An increased number of young connective tissue cells is also noted.

The usual pathologic picture is that of a long-standing lesion with proliferation of endothelial cells and fibroblasts, which form extensive thrombi in both veins and arteries. The internal elastic lamina is usually well preserved, the medial coat contains fibroblasts, endothelial proliferation is present, the muscle fibers are well preserved, and there is extensive fibroblastic proliferation in the adventitia. There is no necrosis of the vascular walls. The most striking histologic finding is the extensive proliferation of endothelial and fibroblastic cells, which permits the pathologist to differentiate among thrombo-angiitis obliterans, polyarteritis nodosa, simple arterial thrombosis, and arteriosclerosis obliterans.

CLINICAL DIAGNOSIS

The clinical diagnosis of thrombo-angiitis obliterans is much more difficult. The patient usually has been treated for arthritis, flat feet, neuritis, and many other disorders before it is recognized that circulation is inadequate. Uusually, this is not

recognized until gangrene has developed, when amputation may be the only remaining procedure. This is most disturbing to those of us interested in peripheral vascular disease, because thrombo-angiitis obliterans is not difficult to diagnose.

The greater percentage of cases occur among young men, although occasionally the disease may occur among females. Rarely does thrombo-angiitis obliterans occur among non-smokers.

Symptoms—The patient usually complains of abnormal fatigue or pain in calf muscles on exercise, which is relieved by rest. The patient frequently complains of numbness, paresthesia, cold fingers and toes, diminution in perspiration of the affected part, brittleness of the nails, and color changes, especially on dependence. These patients note that their feet become fiery red when held in a dependent position.

Even a superficial examination will reveal inadequate circulation. Arterial pulsations are siminisheh or absent in the involved extremity. The color changes consist of blanching on elevation and redness on dependence. Occasionally, superficial phlebitis is present. The combination of these physical findings in a young man who smokes and has painful extremities, especially after exercise, is sufficient for at least a tentative diagnosis of thrombo-angiitis obliterans.

ETIOLOGY

In spite of the voluminous literature on this disease since it was described by Leo Buerger in 1908, the etiological factors are still a mystery. It is not known whether thrombo-angiitis obliterans is an inflammatory disease or a sensitivity reaction. Some investigators believe that tobacco is a causative factor. Others feel that infection is the major cause. Although the disease is a pathologic entity, this does not mean that a common etiologic factor must be present in all cases.

It is possible that several of these factors, such as infection, virus, or tobacco, may produce the disease in an occasional person whose vessels are particularly sensitive or susceptible and capable of reacting by an excessive proliferative response of the endothelial and fibroblastic cells. I am inclined to believe that this disease is a sensitivity reaction similar to polyarteritis nodosa, serum sickness, and lupus erythematosis. In the light of present knowledge, it must be admitted that no one actually has any idea of the true cause of thromboangiitis obliterans.

TREATMENT

Early cases—The primary object in treatment is to recognize the disease before gangrene develops. These patients have intermittent claudication, which usually may be relieved by their discontinuing smoking, meticulous care of the feet, use of mild fungicides to eradicate infection about the toes, careful chiropody of the nails, corns and calluses, limitation of walking within the limits of the patient's circulation reserve (this means that if the patient develops claudication after walking one block, he should only walk a half block), lukewarm tub baths in at least 12 inches of water every night, daily massage of the legs, and alcoholic drinks in small quantities several times daily.

A nitroglycerin tablet, 1/400 gr., under the tongue three times a day is advised, as I believe this causes vasodilatation of the small collateral vessels in the peripheral vascular system. Roniacal seems to be an adequate vasodilator; it tends to break down after absorption into nicotinic acid, so therefore has a more prolonged action in the body than nicotinic acid given orally. The dose

is 50 mg. given three times a day.

Advanced cases — In the late stages of the disease, if gangrene has developed or severe pain while at rest is present, the problem is more difficult. The patient must be hospitalized. Large doses of antibiotics are indicated to localize and prevent spreading infection. Sympathectomy may at times prevent amputation. Nerve-crushing procedures may be helpful, as oftentimes it relieves the pain in an infected gangrenous extremity so the patient will be able to stand applications to the affected part. Whirlpool baths at times will aid healing of localized infection or gangrene.

We have not been successful in the treatment of thrombo-angiitis obliterans complicated by gangrene with either priscoline, hypertonic saline solutions, intra-arterial histamine or intravenous ether injections. The administration of intravenous typhoid vaccine in graduated doses three times weekly has been worthwhile in an occasional case.

SUMMARY

The combination of the treatment outlined for an ambulatory case, with the addition of the surgical procedures for the more severe cases, has been successful in saving the extremities in cases of thrombo-angiitis obliterans. We have found that close cooperation between the surgeon and internist gives the patient a better chance for recovery.

Isonicotinic Acid Hydrazide –

(Continued from page 415)

(perhaps as an adjunct to streptomycin) in the treatment of tuberculous meningitis and also miliary tuberculosis.

Ominous, however, is the apparent ease with which the tubercle bacillus becomes resistant to this drug. The full import of this development cannot yet be stated. Workers at the Trudeau Sanitarium have reported that of 38 tuberculous patients treated with the drug, eleven became resistant to it. Dr. N. D. D'Esposo, chief of the tuberculosis service of the Veteran's Administration Hospital at Summit, New York, has expressed his unwillingness to employ the drug because of the risk of resistance developing. Pending further clarification of the susceptibility of the drug in this respect, its indiscriminate use must be condemned

No serious toxic effects of the drug in man have as yet been reported even with doses as high as 10 mg. per kilogram of body weight (the usual dose is about 4 mg. per kg. of body weight. The side effects which have been attributed to the drug are predominantly neurologic, and include hyperreflexia, vertigo, constipation, muscular twitchng, delay in micturition, urethral anesthesia, paresthesia of the extremities, dryness of the mouth, insomnia or restlessness, skin rashes and transient loss of memory. It must be remembered that the treatment of tuberculosis is a long-term process and that no large series of patients treated over a long period of time with this new drug is as yet available.

AIDS IN DIAGNOSIS

Agglutination Test for Rheumatoid Arthritis

This test involves the agglutination of sheep's erythrocytes sensitized with hemolytic serum. Horse serum was generally used for this purpose, although erythrocytes and serum from other species are equally reliable. The patient's serum in dilutions of 1:10 to 1:20 was added to the sensitized cells and incubated for one hour at 37° C. The end-point was taken as that serum dilution which gave agglutination just visible to the naked eye. Accepting a titer of 1 in 30 as normal, the titer was found to be elevated in 85 per cent of the patients with rheumatoid arthritis, and in only 13 per cent of the control specimens from patients with other diseases. Destruction of the fourth component of the serum complement removed agglutinating activity from the serum.

(D. Hobson and R. H. Gorrell, *Lancet*, 1: 398, 1952.)

Blood Sedimentation Rate

"The red blood sedimentation rate is the simplest and best method for recognizing the possible presence of hidden cancer or cryptogenic infections or for following the course of disease such as arthritis." Author prefers the Westergren technic bevause of its wide range between normal and abnormal. "A reading up to 20 mm. is usually normal; figures around 36 mm. are often seen in arthritis; figures around 50 mm. are common with rheumatic arthritis or chronic ulcerative colitis, and from 50 to 120 mm. are seen in cases of cancer."

(Editorial by Walter C. Alvarez. Mod. Med., March 1, 1952. p. 10)

Guide Catheterization and Radiography

The catheterization is carried out with a plastic catheter which has inside of it a metallic guide with a flexible terminal end. The heavy shadow cast by this instrument makes a good orientation under the screen possible. In experiments on dogs, the femoral vein or artery were principally used as approaches to the side branches of the inferior vena cava or the abdominal aorta. Good visualization of normal and abnormal vascular patterns in the liver, spleen and kidney was obtained with small amounts of skiagraphic material.

This method of catheterization also makes possible the direct application of drugs, antibiotics, radioiosotopes, and so forth, to the diseasd organs.

(A. M. Rappaport, *Can. Med. Assn. J.*, 67: 93-100, August 1952.)

Adrenocortical Function in Portal Cirrhosis

Adrenocortical function was assayed in ten patients with portal cirrhosis by measurements of the 24-hour 17-ketosteroid excretion, eosinophil response to adrenalin, and the hyaluronidase fluorescin test. On the basis of these tests, eight of the patients with advanced portal cirrhosis showed inadequate adrenocortical function. Two patients with past evidence of hepatic impairment but relatively normal liver function at the time showed little or no evidence of functional impairment of the adrental cortex.

(A. J. Finestone and C. R. Shuman, *Am. J Clin. Path.*, 22: 384, 1952.)

Bronchial Stenosis

The author contends that the slowly developing stenosis of the bronchi does not produce for a long time subjective or objective symptoms. After obstruction is complete, the result invariably is atelectasis followed by infection. The prognosis is poor if the stenosis is not removed. The most important signs and symptoms of the three clinical stages of development are: 1) a cough and repeated hemorrhages; 2) pneumonic and pleuritic attacks and localized emphysema; 3) gangrene, empyema, and bronchiectasis. The following diseases may be responsible for stenosis of the bronchi: 1) bronchial carcinoma; 2) pulmonary adenoma; 3) bronchial tuberculosis; 4) non-specific inflammations. The author stresses that for a successful early diagnosis, tomography, bronchography and bronchoscopy are necessary.

(R. Schoen, Dt. Med Wschr. 14:433, 1951). (J. V. Boros. Heart. Die Med. Welt. 12:376, 1951).

Cardiac Hypertrophy

The author emphasizes that greater effort is followed by diastolic "Tonogenic Dilatation" of the muscle fibers of the heart. If the increased reserve power of the muscle is exhausted, muscular weakness is the consequence with "Myogenic Dilatation" of the muscle fibers which again leads to cardiac hypertrophy. This process is not a physiological adaptation but a pathological process. With increasing hypertrophy, a disproportion of blood supply and muscular mass will ensue which brings about anoxemia of the heart muscle. The author stresses that any hypertrophic heart, even the hypertrophic athletic heart, must be considered a muscularly damaged heart, the reserve power of which is diminished.

(J. V. Boros. Heart. Die Med. Welt. 12:376, 1951).

Costen's Syndrome

As a rule, the patient presents one or several of the following symptoms: 1) pain within or about the ears; 2) tinnitus; 3) stuffy sensation in ears; 4) mild deafness relieved by inflation of eustachean tubes; 5) tenderness on the temporomandibular joints; 6) sinus headaches; 7) disturbance of movement of temporomandibular articulation; 8) neuralgia; 9) burning or prickling sensation of tongue, throat, side of nose, sometimes accompanied by a light herpes. On examination the gross findings are loss of molar teeth, ill fitting dental plates, uneven movement of the lower jaw, tenderness of the mandibular joints to palpitation, presence of trismus. The x-ray findings are density changes in the mandibular joint, widening of the joint spaces, erosion of the interior surface of the condyle, fracture of the tympanic plate, impacted unerupted third molar teeth. In the treatment of Costen's syndrome a dentist should always be consulted.

(A. C. Poweleit, M. J. Ky. State Med. Assn., 11: 494. 1951)

Hypotassemia

Hypopotassemia may be due to abdominal surgery, starvation, inanition, alcoholism, vomiting, diarrhea, Wangenstein suction. The clinical signs are: generalized weakness, hypotonia that may lead to flaccid muscle paralysis, hypotension (especially diastolic), clouding of sensorium, shallow and rapid respirations. The EKG is pathognomic: prolongation of electrical systole as measured by the lengthening of the Q-T interval. All these changes are completely reversed by administration of solution containing 2 Gm. of KCL per dram.

(Wm. A. Steiger. Pennsylvania Med. J. 54:866, September 1951).

THERAPEUTIC TRENDS

Chloramphenicol in Wound Infections

It is rather exceptional by now to find a strain of *Staphylococcus aureus* which is susceptible to either penicillin or streptomycin. Chloramphenicol, on the other hand, has proved itself a most useful antibiotic for both ulcers and wound infections. This conclusion of the authors is based on their experience with 30 consecutive cases of infected burns, varicose veins and abscess cavities, all of which were treated successfully by the local application of 5 per cent chloramphenicol. Bacterial clearance was obtained in all instances within an average time of 4 to 5 days. The preparation was used either as a powder in lactose or as a solution in propylene glycol.

(M. H. Flint, H. Gillies, and D. A. Reid, *Lancet*, 1:541-544, March 12, 1952).

Glaucoma

Glaucoma is a common source of blindness. New knowledge of how the aqueous humor of the eye is formed has brought a new concept of the pathology of this disease. Intra-ocular fluid comes partly by diffusion from neighboring blood vessels and partly from secretion from specialized cells within the eye. It is secretion which maintains normal intra-ocular pressure and flow. Changes in intra-ocular pressure depend chiefly on changes in blood flow in the local vessels, which are under nervous control and can be studied *in vivo* through plastic windows inserted in the eye-ball.

Glaucoma in its early stages is due to an instability of nervous vascular control leading to spasmodic rises of intra-ocular tension and consequent compression of the optic nerve.

This study (*i.e.*, by the Medical Research Council) has also shown that drugs must be fat-soluble to pass from the blood into the inner eye, which explains why penicillin is ineffective in deep infection of the eye and why chloramphenicol is effective. Cortisone also penetrates readily and therefore is very valuable in controlling acute inflammation of bacterial, allergic or traumatic origin.

Cited in *Brit. Med. J.*, 2:211, July 26, 1952).

Lymphoid Hyperplasia of the Nasopharynx

Irradiation has been used frequently in reducing hyperplasia of lymphoid tissue in nose and pharynx. It is applied in cases of impaired hearing and of chronic upper respiratory infection. The following types of irradiation have been employed: 1) beta radium applicator which is the newest device; 2) the radon applicator; 3) x-ray irradiation. For a very small amount of lymphoid tissue surrounding the orifice of the eustachian tube, the radium applicator would be the most desirable type. According to the author, there are no reports of permanent damage in the nasopharynx following irradiation with the beta ray applicator.

(J. B. Irvin, Calif. Med., 3:198, March, 1951).

Effects of Procaine Amide on the Heart

Experimental and clinical studies prompted the authors to draw the following conclusions with respect to the actions of procaine amide on the heart:

1. It increases the threshold of excitability and slows the speed of conduction in both auricles and ventricles.

2. It has little effect on auriculo-ventricular conduction while the sinus rhythm is maintained.

3. Impairment of atrio-ventricular and intra-ventricular conduction is greater when the rate of the pacemaker is higher.

4. Administration of procaine amide given in equal doses has a greater effect on intra-ventricular conduction when administered in a single intravenous injection than in slowly administered venoclysis.

5. Procaine amide is effective in auricular disorders. It clears up auricular extrasystoles and supraventricular paroxysmal tachycardia, and can slow down the rate of auricular fibrillation or flutter. Since paroxysmal auricular tachycardia responds favorably to acetylcholine or its derivatives, the use of procaine amide should be reserved for cases in which acetylcholine is ineffective or contraindicated.

6. Procaine amide is the drug of choice in arrhythmias of ventricular origin (extrasystoles, ventricular flutter, and paraxysmal ventricular tachycardia). Because it is active either orally or intravenously, it should be administered by either route according to the severity of the case.

7. In instances of auricular flutter, the use of procaine amide is dangerous because it can lead to a 1:1 atrio-ventricular response with aberrant intra-ventricular conduction, eventually inducing ventricular flutter or fibrillation. In instances of paroxysmal auricular fibrillation, procaine amide may re-establish a sinus rhythm but it does not seem to be completely without danger.

8. In the treatment of arrhythmias caused by overdosage of digitalis or its derivatives, it should be kept in mind that while procaine amide can clear up ventricular extrasystoles produced by digitalis, its improper use can favor the occurrence of ventricular flutter or ventricular fibrillation. This danger may be reduced by giving procaine amide by a slowly administered venoclycis, while constantly checking the electrocardiogram.

(J. Zapato-Diaz, E. Cabrera, and R. Mendez, *Am. Heart J.*, 43:854-870, June, 1952).

Treatment of Pelvic Abscesses

The method consists in the simple aspiration of a pelvic abscess and injection of antibiotics into the abscess cavity. The method was applied successfully by the author to fourteen patients with pelvic abscesses. The purulent material was aspirated through the pouch of Douglas, followed by injection into the abscess cavity of one million units of penicillin and 2 Mm. of streptomycin. Nine of the patients were adjudged seriously ill. All had marked lower abdominal tenderness. In only two instances of chronic infection, of which the abscess had been an exacerbation, was it necessary to have recourse to further surgery, but even in these two cases no evidence of abscess was present at the time of laparotomy. The average hospital stay was 10 days, and all of the patients were discharged symptom-free.

(W. R. C. Tupper, *Canad. Med. Assn. J.*, August 1952, (v. 67) pp. 147-148.)

Reactions to Immunization

Neurological complications from rabies vaccine may extend from transient neuritis to fatal involvement of the central nervous system. The recent production of rabies vaccine from virus cultured embryonated duck eggs may cause fewer reactions. Complications from small pox vaccination can be avoided by using aseptic technic and by making the insertion superficially. Post-vaccination encephalitis has occurred much less frequently in this country than in Europe.

Severe reactions to pertussis vaccine are rare but may be serious. Convulsions with or without fever sometimes develop. About 53 cases of brain damage following pertussis immunization have been published in this country. Diptheria toxoid generally does not cause reactions in children. In adults the Moloney skin tes tshould be performed before vaccination.

Tetanus toxoid is one of the least reactive of the biologicals. Most of the currently available tetanus toxoid is made by the Pillemer process and is practically free from nonspecific fractions. It has been observed that poliomyelitis may occur after immunization and that paralysis was more prevalent in the inoculated extremity.

The New York State Department of Health reported that in 1950 poliomyelitis was twice as frequent in patients who had received some kind of injection one month or less before onset. Similar findings have been reported from a Minnesota epidemic. The New York State Board of Health has recommended that all elective immunizations should be withheld during the months of June, July, August, September and October.

Physicians Bulletin. 1:7, 1952

Pseudomonas Aeruginosa Infections

Pseudomonas Aeruginosa was previously known as bacillus pyocyaneus. It is a normal inhabitant of the human intestinal tract and comes to the fore only when the normal coliform flora has been suppressed by antimicrobial drugs. In mixed infections it may contribute to the chronicity of the process. When it reaches the blood stream through massive seeding from a focus it may result in sepsis. Chemotherapy has been difficult. The authors report that treatment with polymyxin B (2.1 mg. per kilogram of body weight, daily, intramuscularly) effects good results. This drug is the most active agent available at present for the treatment of these infections and also is safe for topical and parenteral administration.

(E. Jawetz, Arch. Int. Med., 1:90. 1952).

Tuberculosis

The American Trudeau Society has published a case report on anti-microbial therapy in tuberculosis. The following conclusions have been reached: drug therapy alone is an inadequate treatment for tuberculosis; antimicrobial drugs should be administered only within an overall program of surgical and medical treatment; this treatment should be given in a tuberculosis hospital or a tuberculosis ward of a General Hospital. It is advisable to administer simultaneously combinations of antimicrobial agents in order to delay the emergence of drug-resistant striens of tubercle bacilli. The best combination is that of one of the streptomycin drugs with para-aminosalicylic acid (PAS).

(Am. Trudeau Society, American Review, Tuberculosis, 63:617, 1951)

Report of a Case: – Cardiac Neurosis

A man aged 21 years had been rejected by the Army several years previously because of flat feet, a "bad heart" and hypertension. The patient was later examined by his family physician, who told him that his condition was satisfactory. Three years later he was rejected by an insurance company, when he again consulted a private physician.

The patient's parents and two brothers were in apparent good health. The patient, an agricultural worker, weighed 170 pounds and was 5 feet, 9 inches tall. His weight had remained the same with exception of a slight loss following tonsillectomy performed five years previously. He was somewhat disturbed because he had been rejected by the Army and an insurance company because of a heart condition.

He had no subjective complaints. Objective findings as to the gastrointestinal system, the respiratory system, the nervous system, and the genioturinary system were essentially negative.

Examination of the cardiovascular system revealed the following: The heart appeared to be normal in size and shape; the apical, aortic and pulmonary sounds were of equal intensity and no murmurs were heard. The pulse rate was 84 per minute, regular and of good quality. The blood pressure in the right arm was 135/80 and in the left, 132/72. Examination of the ocular fundi revealed normal arteries and veins; all peripheral vessels were normal with good pulses, including the dorsal pedis and tibialis.

The electrocardiogram showed a slight left axis deviation, P wave notched and diphasic in lead 3, QRS complex notched in lead 3, T wave was inverted in lead 3, no extrasystoles, and lead 4 normal. The examining physician concluded that not only were the electrocardiographic findings essentially normal, with exception of the left axis deviation, but that the condition of the patient did not display any underlying pathologic condition which would prevent him from entering the military service or from receiving a standard life insurance policy.

One staff physician interpreted the electrocardiogram in a somewhat different way as follows: left axis deviation, P wave notched and diphasic in lead 3, QRS notched in lead 3 and T wave inverted in lead 3 would not permit the diagnosis of an entirely normal electrocardiogram. The findings would suggest some possible damage to the myocardium, which, from results of the complete examination, was now healed. This physician thought that at the time of the Army examination there may have been consistent reasons in declining him, while at the time of the insurance examination there was no essential reason not to grant insurance protection.

Another physician voiced the opinion that the findings suggested the presence of cardiac neurosis at the time of the Army examination rather than organic heart disease. A third physician supported this view, and stated that it may be presumed that the "bad heart" was a casual way of describing a cardiac neurosis and that the etiologic factors of the hypertension were emotional disturbance and fear. His rejection for insurance several years later was probably because examination again provoked the original protective pattern.

NEW PHARMACEUTICAL PRODUCTS

Manncor: A scored tablet, containing mannital hexanitrate, 30 mg.; phenobarbital, 15 mg.; rutin, 50 mg.; and ascorbic acid, 50 mg.

Used in: Stabilization of blood pressure and sedation.

Dosage: One tablet daily for 2 days; then 2 tablets in 4 doses daily for 1 week; after 1 week, 3 tablets daily for 4 weeks, then stop Manncor and use sedatives only for 7 to 10 days. Then repeat cycle.

Chicago Pharmacal Company, Chicago, Illinois.

Lipomic: A tablet, containing methionine, 50 mg.; choline dihydrogen citrate, 123 mg.; inositol, 25 mg.; and liver concentrate (N.F.), 60 mg.

Used In: Fatty infiltration of liver, hepatitis, cirrhosis, atherosclerosis.

Dosage: Ten tablets daily.

Chicago Pharmacal Company, Chicago, Illinois.

Salcorbine: A tablet containing sodium salicylate, 5 gr.; ascorbic acid, 100 mg.; and colchicine, 1/150 gr.

Used In: Atrophic and hypertrophic arthritis, gout.

Dosage: Two tablets after each meal and on retiring.

Chicago Pharmacal Company, Chicago, Illinois.

Cream Phenergan Hydrochloride: A disappearing cream containing N-(2'dimethylamino 2'methyl) ethyl phenothiazine hydrochloride.

Used In: Prevention of itching.

Dosage: 3 or 4 times daily.

Wyeth Incorporated, Philadelphia, Pennsylvania

Injection Wyamine Sulfate: A sterile, aqueous solution containing N-methylphenyl-tertiary-lutylamine.

Used In: Hypotensive states not associated with hemorrhage.

Dosage: Intravenously or intramuscularly, as necessary.

Wyeth Incorporated, Philadelphia, Pennsylvania

Phenergan Expectorant with Codeine: A cough syrup.

Used in: Cough associated with common cold or minor throat irritations.

Dosage: One teaspoonful (5cc.) every 4 to 6 hours. In persistent night cough, 2 teaspoonfuls before retiring.

Wyeth Incorporated, Philadelphia, Pennsylvania

Acorto Gel: Long-acting form of ACTH in a mixture of 20 per cent gelatin with 30 per cent propylene glycol and 0.5 per cent phenol. Designed to exert therapeutic effects over a prolonged period, reducing frequency of injections to one or two times a day

Used In: Rheumatoid arthritis, acute rheumatic fever, ulcerative colitis, and allergic manifestations.

Dosage: In patients beginning treatment, 40 I.U. twice daily. Maintenance treatment generally requires 20 to 40 I.U. or less per 24 to 48 hours.

George A. Breon & Company, New York 18, New York

Hy-Tape Plastic Adhesive Tape: Tape of tissue-thin plastic for use whenever conventional tape is employed.

Advantages: Water proof, washable, pliable.

Hy-Tape Corporation, New York 32, New York